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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,545	05/18/2005	Eric Ferrandis	427.096	7587

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HEDMAN & COSTIGAN P.C.
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
12/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,545	FERRANDIS, ERIC	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5 and 8-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2-5 and 8-10 are all the pending claims for this application.

2. Claims 1, 6, 11 and 18-22 were cancelled and Claims 2, 3 and 10 were amended in the Response of 11/26/08.

3. Claims 2-5 and 8-10 are all the pending claims under examination.

4. The indicated allowability of claims 4, 5, 8 and 9 is withdrawn in view of the newly discovered reference(s) to Ferrandis et al. (USPN 7385024) and Campbell, Biology, 3rd Ed (p. 321). Rejections based on the newly cited reference(s) follow.

5. This Office Action contains new Grounds for Rejection, and therefore the finality of the Office Action of 8/27/08 is withdrawn.

Withdrawal of Objections

Specification

6. The objection to the improper use of trademarks in this application has been addressed in the Response of 11/22/08. The amendments to the specification on p. 3 of the Response of 11/26/08 are acknowledged.

Claim Objections

7. The objections to Claim 10 for the following apparent typographical errors are withdrawn:

a) at line 6, "immunoligical and/or" has been amended to recite "immunological and/or".

b) at lines 14-15, "protein human GHRN protein" has been amended to recite "a protein binding human GHRH."

c) the typographical error in the phrase "one of the fragments of *the said* SEQ ID NO:13" is moot in view of the deletion of the phrase from the claim.

Withdrawal of Rejections

Claim Rejections - 35 USC § 112, second paragraph

8. The rejection of Claims 1 and 19 for the recitation "or one of its fragments" in Claim 1 is moot for the cancelled claims.

9. The rejection of Claim 10, lines 5 and 13 for the recitation "or one of the fragments of the latter" is moot for the deletion of the phrase from the claim.

Claim Rejections - 35 USC § 112, first paragraph

Written Description

10. The rejection of Claims 1, 10 and 19 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reciting polynucleotide fragments of a polynucleotide comprising SEQ ID NO: 8 (Claim 1) or SEQ ID NO: 9 or SEQ ID NO:13 (Claim 10) is moot for cancelled Claims 1 and 19 and withdrawn for amended Claim 10 in view of the deletion of the reference to fragments.

Enablement (1)

11. The rejection of Claims 1, 10 and 19 under 35 U.S.C. 112, first paragraph, in lacking enablement for just any polynucleotide fragment is moot for cancelled Claims 1 and 19 and withdrawn for amended Claim 10 in view of the deletion of the reference to fragments.

Enablement (2)

12. The rejection of Claim 19 under 35 U.S.C. 112, first paragraph, in lacking enablement for using the polynucleotide in gene therapy is moot for the cancelled claim.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 10, lines 3-4 is indefinite for the recitation "or by a sequence complementary to the polynucleotide sequence SEQ ID NO:9" because the complementary sequence is necessarily an anti-sense strand for the sequence of SEQ ID NO:9 and it is not clear how a functional polypeptide having "at least one immunological and/or biological activity" could be encoded by and expressed by the

anti-sense or complementary strand. A dictionary definition for a "complementary" strand from the on-line Free Dictionary is provided (pp. 1-3). The art recognizes the terms "complementary" and "antisense" as being interchangeable, and accordingly, that the complementary strand would not yield a functional protein.

b) Claim 10, element a) recites the limitation "the sequence complementary to the polynucleotide sequence...or SEQ.ID.NO. 13." There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 2-5 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrandis et al. (USPN 7385024; issued June 10, 2008; filed 2/26/02) in view of

Campbell (Biology, 3rd Ed, the Benjamin/Cummings Publishing Company, Inc., 1993 (p. 321)) and Sambrook et al. (Molec. Cloning, Vol 2, Protocol 1, pp. 8.18-8.22 (2001)).

Claims 2-5 and 8-10 are interpreted as being drawn to isolated polynucleotide of SEQ ID NO:8 (cDNA for heterocarpine; Claim 2), isolated polynucleotide of SEQ ID NO:9 (open reading frame of cDNA for heterocarpine; Claim 3); isolated polynucleotides for sequences SEQ ID NOS: 4/5 and SEQ ID NO:11/12 (primers used in PCR reactions for heterocarpine cloning; Claim 4); isolated polynucleotide of SEQ ID NO:13 (SEQ ID NO:9 having artificially undergone deletion of the initiation codon ATG and the stop codon; Claim 5); an expression vector containing the polynucleotide of SEQ ID NO:13 (Claim 8); a host cell transformed or transfected with the expression vector of Claim 8 (Claim 10); and a process for producing a polypeptide encoded by the polynucleotide sequence of SEQ ID NO: 9 or 13 comprising culturing a host cell transformed or transfected with the expression vector under conditions to express the polypeptide and isolating the polypeptide from the host cell cultures.

The isolated cDNA, the ORF for the cDNA, vectors and methods for expressing the recombinant protein for heterocarpine was prima facie obvious at the time of the invention over Ferrandis, Campbell and Sambrook.

Ferrandis describes the isolation of a protein called heterocarpin from Pilocarpus heterophyllus plant cells. This protein has a molecular weight of approximately 90.9 kDa and comprises fragments of the peptide sequences, SEQ ID Nos 1-3. Furthermore, the heterocarpin of Ferrandis having SEQ ID NO 10, is coded by the fragment of the polynucleotide having the polynucleotide sequence SEQ ID NO:8

contained between the bases in positions 115 (ATG initiator codon) and 2437 (UAA stop codon), i.e. by the polynucleotide sequence SEQ ID NO:9. Ferrandis discloses that heterocarpin binds human GHRH and can be used to antagonise the effects of GHRH, to treat proliferative diseases (cancer), and to treat diabetic retinopathies and nephropathies. Ferrandis does not disclose cloning the cDNA or ORF for heterocarpine, but the ordinary artisan would not have had any particular difficulty in cloning heterocarpine in view of Campbell.

Campbell teaches the nucleic acids which encode the amino acids are well known in the art. Therefore the ordinary artisan could readily envisage all nucleic acids that would encode any protein sequence.

Sambrook (Protocol 1) teaches PCR strategy for cloning genes and using primer sets to perform these operations.

The ordinary artisan would have been motivated and been assured of success in having cloned the heterocarpine cDNA, inserted it into a vector and expressed the recombinant protein at the time of the invention over Ferrandis, Campbell and Sambrook. Ferrandis teaches the protein sequence for heterocarpin, and the medical interest for this protein, therefore a person skilled in the art, aware of the information disclosed in Campbell and Sambrook would have found more than sufficient motivation to have cloned heterocarpine using primer sets corresponding to the primers of SEQ ID NO:4/5 and 11/12 to obtain the cDNA and ORF as well as subcloning the cDNA or ORF into an expression vector for expressing the recombinant protein without having to exercise any inventive skill. The ordinary artisan would have been reasonably assured

of success in having cloned and isolated the heterocarpine cDNA and expressed the clone to produce a recombinant protein because the field of art for cloning and cDNA expression of proteins was well established at the time of the invention based on the disclosures of Campbell and Sambrook. For all of these reasons, the claimed invention was prima facie obvious.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lynn A. Bristol/
Partial Signatory Authority